HYPERSENSITIVITY REACTIONS

Step 1: NBME 17 to 31

Type 1

NBME 31

A 27-year-old woman is admitted to the hospital because of a 1-week history of lower abdominal pain that became more severe 2 days ago. She also has had fever, nausea, and vomiting. Her temperature is 38.4°C (101.2°F), pulse is 110/min, and blood pressure is 135/90 mm Hg. Abdominal examination shows tenderness in the right lower quadrant to light palpation and percussion. A CT scan of the abdomen with oral and intravenous contrast is obtained. Shortly after having the test, she develops audible wheezing in all lung fields and the rash shown in the photograph. Her pulse now is 120/min, and blood pressure is 90/65 mm Hg. Which of the following best describes the mechanism of this patient's skin reaction?

A) Cytokine release from segmented neutrophils
B) Direct activation of mast cells
C) IgE antibody release from eosinophils
D) Increased production of bradykinin
E) Systemic entry of bacterial endotoxins

Correct Answer: B.

Direct activation of mast cells causes degranulation and release of vasoactive substances, including histamine, that produce symptoms ranging from uncomplicated urticaria to severe anaphylaxis. Symptoms of anaphylaxis include urticaria, vasodilation leading to hypotension, compensatory tachycardia, and angioedema. Although rare, intravenous contrast used for CT scans may cause direct mast cell degranulation, leading to an anaphylactic/anaphylactoid reaction. Anaphylactic reactions commonly occur due to the presence of preformed IgE antibodies against an antigen. IgE antibodies promote activation

and degranulation of mast cells. Regardless of the inciting mechanism of mast cell activation and degranulation, histamine release leads to the final common pathway characterized by the signs and symptoms of anaphylaxis. Recognition and treatment of anaphylaxis with epinephrine is critical to prevent life-threatening complications, including airway obstruction, respiratory arrest, and cardiovascular collapse from distributive shock.

Incorrect Answers: A, C, D, and E.

Cytokine release from segmented neutrophils (Choice A) is triggered by the innate immune response. Cytokines produced by neutrophils promote inflammation and recruit additional inflammatory cells, however, they are not responsible for anaphylaxis.

IgE antibody release from eosinophils (Choice C) is incorrect. IgE antibodies, along with all other types of antibodies, are produced by plasma cells after class switching. The binding of IgE to receptors on mast cells triggers mast cell degranulation and release of vasoactive substances, including histamine. Although this reaction may trigger anaphylaxis in cases of food allergies or bee stings, intravenous contrast has been demonstrated to trigger mast cell degranulation independent of IgE.

Increased production of bradykinin (Choice D) would promote vasodilation and increase permeability in capillary beds, but it would not trigger an anaphylactic reaction. Increased bradykinin levels could lead to an angioedema-type presentation, often seen in patients with ACE inhibitor intolerance.

Systemic entry of bacterial endotoxins (Choice E), such as toxic shock syndrome toxin released by *Staphylococcus aureus*, can cause fever, hypotension, and tachycardia in affected patients. The presence of such toxin also mediates staphylococcal scalded skin syndrome, which generally presents with erythroderma and skin sloughing.

Educational Objective:
Direct degranulation of mast cells from intravenous contrast causes release of intracellular vasoactive substances, including histamine. Histamine release promotes urticaria, vasodilation, compensatory tachycardia, and angioedema in patients with anaphylaxis. Recognition and treatment of anaphylaxis with epinephrine is critical to prevent life-threatening complications, including respiratory arrest and cardiovascular collapse.

🧠 **Key First Aid Summary Points**

- **IV contrast can directly activate mast cells**
- **Non–IgE-mediated anaphylaxis = pseudoallergic reaction**
- **Histamine is the final common mediator**

🎯 NBME Question Strategy Tip

- *IV contrast + rash + hypotension = mast cell degranulation,* even **without prior sensitization or IgE**.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"27-year-old woman... lower abdominal pain... more severe 2 days ago"	Abdominal infection/inflammation concern	+ Subacute pain worsening	Incidental setup – not core to current reaction
"Fever, nausea, vomiting… temp 38.4°C, pulse 110/min"	Likely infection (e.g., appendicitis, PID)	+ Fever, tachycardia	Suggests systemic inflammation (background setup)
"Tenderness in RLQ to light palpation and percussion"	Appendicitis/PID still possible	+ Localized peritonitis	Not related to current allergic reaction
"CT scan of the abdomen with oral and IV contrast"	**IV contrast is key trigger**	+ Known anaphylactoid agent	High-yield cause of pseudoallergic reaction
"Shortly after… wheezing… rash (urticaria)"	Classic **anaphylactic** presentation	+ Wheezing, rash	Mast cell mediator effect
"Pulse now 120… BP 90/65"	Cardiovascular collapse = **anaphylaxis**	+ Tachycardia, hypotension	Histamine → vasodilation/shock

❌ **Distractor Analysis Table**

Answer Choice	Alluded Diagnosis	Why It's Incorrect Here
A. Cytokine release from segmented neutrophils	Sepsis/SIRS or bacterial inflammation	Not acute-onset with rash/hypotension; no infectious toxin
C. IgE antibody release from eosinophils	IgE-mediated allergy (e.g., food, bee sting)	IgE made by **plasma cells**, not eosinophils; not required in this reaction
D. Increased bradykinin production	ACE inhibitor–induced angioedema	No ACE inhibitor history; **urticaria** and wheezing = not bradykinin-mediated
E. Systemic bacterial endotoxins	Toxic shock syndrome, sepsis	No mention of rash pattern like desquamation or tampon/device use
✅ **B. Direct mast cell activation**	**Pseudoallergic** IV contrast reaction	Sudden urticaria, hypotension, wheezing = non-IgE mast cell degranulation

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🧻 **Illness Script: Pattern Recognition Aid**

If you see sudden urticaria + hypotension + IV contrast use → **then think direct mast cell activation (non-IgE anaphylaxis)**

NBME 30

A 32-year-old woman comes to the physician because of a 7-day history of sneezing, nasal stuffiness, and watery eyes. She has a history of similar symptoms each spring while gardening. Her temperature is 37°C (98.6°F). Which of the following types of cells are most likely to be increased in her nasal secretions as a result of this reaction?

A) Basophils
B) Eosinophils
C) Lymphocytes
D) Mast cells
E) Monocytes

Correct Answer: B.

Allergic rhinitis is characterized by IgE mediated inflammation (type I hypersensitivity) of the nasal mucosa. Inciting allergens result in the cross-linking of IgE on the surface of basophils and mast cells, leading to their immediate degranulation and release of histamine, prostaglandins, and leukotrienes, which results in vasodilation, vascular pooling, and increased vascular permeability. This is followed by the recruitment of a variety of inflammatory cells, predominantly eosinophils, to the nasal mucosa, which can be found in nasal secretions. Common inciting allergens include plant pollens, animal dander, dust, and mold. Patients commonly experience nasal congestion, rhinorrhea, sneezing, nasal pruritus, conjunctivitis, and tearing. Patients with allergic rhinitis may display signs of atopic disease processes, such as asthma or eczema. Treatment includes inhaled nasal corticosteroids, inhaled leukotriene receptor antagonists, and oral antihistamines. Removal or avoidance of the offending allergen is essential to prevent further exacerbations and improve symptoms.

Incorrect Answers: A, C, D, and E.

Basophils (Choice A) and mast cells (Choice D) are important for the initiation of the allergic response. However, they are typically outnumbered by eosinophils in nasal secretions in allergic rhinitis.

Lymphocytes (Choice C), especially T lymphocytes, play a role in the potentiation of the allergic response, but are not as numerous as eosinophils.

Monocytes (Choice E) are important cells in phagocytosis and antigen presentation. They do not play a prominent role in the allergic response.

Educational Objective:
Allergic rhinitis is characterized by IgE mediated inflammation (type I hypersensitivity) of the nasal mucosa. Inciting allergens result in the cross-linking of IgE on the surface of basophils and mast cells, leading to degranulation and release of cytokines, especially of

histamine, prostaglandins, and leukotrienes. This results in the recruitment of a variety of inflammatory cells, predominantly eosinophils, to the nasal mucosa.

🧠 Key First Aid Summary Points

- **Allergic rhinitis = Type I hypersensitivity** (IgE-mediated)
- **Eosinophils dominate** in late-phase allergic responses
- **Mast cells trigger; eosinophils sustain inflammation**

🎯 NBME Question Strategy Tip

- Look for **seasonal symptoms + sneezing + itchy eyes** = IgE allergy → think **eosinophils in secretions**.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"32-year-old woman… 7-day history of sneezing, nasal stuffiness, and watery eyes"	Allergic rhinitis suspicion	+ Sneezing, congestion, tearing	Type I hypersensitivity: IgE + eosinophils
"History of similar symptoms each spring while gardening"	**Pollen = seasonal allergen**	+ Springtime trigger	Recurrent, specific allergen: classic allergic pattern
"Temperature 37°C (98.6°F)"	Rules out infection	– Fever	Allergic rhinitis is **non-infectious** (helps rule out viral URTI)

❌ Distractor Analysis Table

Answer Choice	Alluded Diagnosis	Why It's Incorrect Here
A. Basophils	Early allergic response (circulation)	Present, but fewer in number than eosinophils in **nasal secretions**
☑ **B. Eosinophils**	Allergic rhinitis (late-phase response)	**Most numerous in nasal secretions**; recruited post mast-cell activation

Answer Choice	Alluded Diagnosis	Why It's Incorrect Here
C. Lymphocytes	Chronic inflammation or viral infection	Present, but not dominant in **allergic mucosa**
D. Mast cells	Early-phase allergy mediator	Mast cells **trigger**, but are tissue-resident, **not predominant in secretions**
E. Monocytes	Chronic infection or antigen processing	No role in IgE or eosinophilic allergic rhinitis

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📋 Illness Script: Pattern Recognition Aid

If you see seasonal sneezing + itchy/watery eyes + pollen exposure → **then think** allergic rhinitis → **eosinophils in nasal smear**

Zaki

NBME 27

A 12-year-old boy is brought to the physician by his mother because of swelling, itching, and redness of his back that began 10 minutes after he was lying in the grass shirtless. Physical examination shows linear edematous eruptions on the back. A secondary mediator of this patient's hypersensitivity reaction is produced by mast cells de novo in response to the allergen. After release of histamine, mast cells will begin de novo synthesis of which of the following substances?

A) C-reactive protein
B) C3b component of complement
C) Interferon alpha
D) Interleukin-1 (IL-1)
E) Prostaglandin

Correct Answer: E.

The patient is displaying signs and symptoms of a type I hypersensitivity reaction to an environmental allergen. The type I hypersensitivity reaction is composed of two phases, the immediate and the late phase. In the immediate phase, preformed IgE on the surface of mast cells and basophils is crosslinked by an antigen leading to their immediate degranulation and release of histamine, which results in vasodilation, vascular pooling, and increased vascular permeability. The late phase typically occurs hours after the initial insult and is mediated by the release of prostaglandins and leukotrienes synthesized by the mast cells. Prostaglandins are derived from arachidonic acid via cyclooxygenase (COX) enzymes. Once released, they modulate cell behavior via interaction with G protein–coupled receptors and activation of intracellular signaling pathways. Type I hypersensitivity reactions may present with symptoms ranging from localized pruritis, edema, and erythema to systemic, life-threatening anaphylaxis. Other examples include allergic asthma, atopic rhinitis, and atopic dermatitis. Skin testing can be performed to identify specific allergens.

Incorrect Answers: A, B, C, and D.

C-reactive protein (Choice A), also referred to as CRP, is an acute phase reactant synthesized by the liver that increases in response to inflammation. Expression of CRP is induced by IL-6. CRP is not synthesized by mast cells.

C3b component of complement (Choice B) is a core component of the complement cascade and is formed by the cleavage of C3. The C3b fragment may then participate in one of three pathways. It may bind with factor B to form C3 convertase and amplify C3 cleavage in a positive feedback loop. It may bind with C4b and C2b fragments to form C5 convertase, or it may opsonize the microbe by binding directly to the pathogen surface. Complement is not synthesized by mast cells.

Interferon alpha (Choice C) is a glycoprotein produced by cells that are infected with a virus. Interferon alpha upregulates MHC expression for recognition and binding with $CD8^+$ T cells, and downregulates protein synthesis to impair viral replication.

Interleukin-1 (IL-1) (Choice D) is a proinflammatory cytokine secreted by macrophages, endothelial cells, dendritic cells, and B lymphocytes. It has numerous effects, including the promotion of fever, vasodilation, and stimulation of endothelial cells to express adhesion proteins for leukocyte recruitment. It is also known as osteoclast-activating factor.

Educational Objective:
Type I hypersensitivity reactions are characterized by an initial histamine release from presensitized mast cells, followed by the synthesis and release of prostaglandins, leukotrienes, and inflammatory mediators.

🧠 Key First Aid Summary Points

- **Type I hypersensitivity = immediate + late-phase**
- **Histamine is immediate; prostaglandins are synthesized de novo**
- **Mast cells release eicosanoids (PGs, LTs)** after activation

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🎯 NBME Question Strategy Tip

- When asked about "**de novo**" mediators in **IgE allergy**, go beyond histamine—think **lipid-derived molecules** like prostaglandins or leukotrienes.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"12-year-old boy… swelling, itching, redness… 10 minutes after lying in grass shirtless"	Timing + trigger → IgE-mediated allergy	+ Acute onset, + allergen exposure	Classic Type I hypersensitivity
"Linear edematous eruptions on the back"	**Wheals** from mast cell histamine → urticaria	+ Rash morphology = dermal edema	Histamine = immediate response
"Secondary mediator… produced de novo by mast cells"	Focus shifts to **late-phase mediators**	+ Key test clue	Think arachidonic acid metabolites (PGs, LTs)

❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. C-reactive protein	Acute phase reactant from liver	Not mast cell–derived; IL-6–induced
B. C3b	Complement opsonin	Not synthesized de novo by mast cells
C. Interferon-alpha	Antiviral cytokine	Secreted by **virus-infected cells**, not mast cells
D. IL-1	Macrophage-derived pro-inflammatory cytokine	Not a primary or secondary **mast cell product**
☑ **E. Prostaglandin**	Mast cell–derived lipid mediator	**De novo synthesized** post–IgE activation (COX pathway)

📋 Illness Script: Pattern Recognition Aid

If you see rapid-onset itchy wheals after allergen exposure → **then think** Type I hypersensitivity → **histamine + prostaglandin**

Zaki

NBME 24

A 32-year-old woman comes to the physician because of a 7-day history of sneezing, nasal stuffiness, and watery eyes. She has a history of similar symptoms each spring while gardening. Her temperature is 37°C (98.6°F). Which of the following types of cells are most likely to be increased in her nasal secretions as a result of this reaction?

A) Basophils
B) Eosinophils
C) Lymphocytes
D) Mast cells
E) Monocytes

Correct Answer - B

Great question. Tough choices. Read the question carefully. They want the result of this reaction. The reaction itself is initiated by mast cell degranulation (allergies). Mast cells release many things and the histamine and eosinophil chemotactic factors are crucial. The result is from later activity by eosinophils, which are activated by IL5. There is IgE clustering and cross linking. Type 1 HSR.

🧠 Key First Aid Summary Points

- Allergic rhinitis = Type I hypersensitivity (IgE-mediated)
- Eosinophils dominate nasal secretions in allergic responses
- Histamine is immediate; eosinophils arrive later

🎯 NBME Question Strategy Tip

- If the vignette uses seasonal allergy symptoms + clear nasal discharge, the correct answer will almost always involve eosinophils, not mast cells or basophils.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
“32-year-old woman… 7-day history of sneezing, nasal stuffiness, and watery eyes”	Strongly suggests allergic rhinitis	+ Classic allergic symptoms	Type I hypersensitivity via airborne allergen

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
“History of similar symptoms each spring while gardening”	Pollen exposure = allergen	+ Recurrent, seasonal trigger	Common cause of IgE-mediated allergy
“Temperature 37°C (98.6°F)”	Rules out infectious cause	– Fever	Helps rule out viral/bacterial URTI

❌ Distractor Analysis Table

Answer Choice	Alluded Diagnosis	Why It's Incorrect Here
A. Basophils	Circulating allergy mediator	Not abundant in local secretions; involved in systemic allergy
✅ B. Eosinophils	Allergic rhinitis late-phase reaction	Recruited to nasal mucosa post–mast cell activation
C. Lymphocytes	Chronic inflammation or viral infection	Not dominant in acute IgE reactions
D. Mast cells	Early allergic response (tissue-resident)	Key for initiation, not found in nasal secretions
E. Monocytes	Chronic infection/phagocytosis	No role in allergic rhinitis pathophysiology

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📜 Illness Script: Pattern Recognition Aid

If you see sneezing + nasal congestion + seasonal exposure → then think allergic rhinitis → eosinophils in nasal secretions

Type 3

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A 23-year-old woman with bone marrow failure is treated with a large dose of rabbit antithymocyte globulin. Ten days later, she develops fever, lymphadenopathy, arthralgias, and erythema on her hands and feet. Which of the following is the most likely cause of these symptoms?

(A) Cytokine secretion by natural killer cells
(B) Eosinophil degranulation
(C) Immune complex deposition in tissues
(D) Polyclonal T-lymphocyte activation
(E) Widespread apoptosis of B lymphocytes

C – Serum sickness! A type III (immune complex) hypersensitivity.

🧠 Key First Aid Summary Points

- Serum sickness = Type III hypersensitivity
- Antigen-antibody immune complexes deposit in tissue
- Complement activation → inflammation (fever, arthralgia, rash)

🎯 NBME Question Strategy Tip

- If symptoms appear 5–14 days after foreign protein exposure (e.g., antithymocyte globulin) and include fever + rash + arthralgia → think immune complex deposition (Type III).

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"23-year-old woman with bone marrow failure treated with rabbit antithymocyte globulin"	Foreign protein exposure (non-human Abs)	+ Serum protein infusion	High-yield cause of serum sickness

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
“Ten days later, she develops fever, lymphadenopathy, arthralgias…”	Delayed hypersensitivity onset + systemic sx	+ Timing + constitutional signs	Serum sickness typically begins 1–2 weeks later
“Erythema on her hands and feet”	Rash due to immune complex vasculitis	+ Rash location (peripheral)	Immune complex deposition → inflammation of small vessels

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❌ Distractor Analysis Table

Answer Choice	Alluded Diagnosis	Why It's Incorrect Here
A. Cytokine secretion by NK cells	Viral defense or tumor surveillance	Not primary in immune complex–mediated disease
B. Eosinophil degranulation	Type I hypersensitivity or parasitic infection	Not relevant to delayed systemic reaction post-foreign protein
✅ C. Immune complex deposition	Serum sickness (Type III hypersensitivity)	Delayed fever, arthralgia, rash after foreign antigen exposure
D. Polyclonal T-lymphocyte activation	Toxic shock syndrome (superantigens)	Requires toxin-producing infection; no context here
E. Widespread B cell apoptosis	Autoimmune or drug-mediated suppression	Doesn't explain systemic inflammatory symptoms or rash

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🧻 Illness Script: Pattern Recognition Aid

If you see fever + arthralgia + rash 1–2 weeks after monoclonal or foreign protein infusion → then think serum sickness → immune complex–mediated Type III hypersensitivity

NBME 29

A previously healthy 16-year-old girl comes to the physician because of a progressive rash over her cheeks and the bridge of her nose during the past 5 weeks. She also has a 1-week history of stiffness of her fingers in the mornings that gradually resolves during the day. A photograph of the face is shown. Serum studies show an antinuclear antibody titer of 1:1280 and C3 concentration of 71 mg/dL (N=100–200). The pathogenesis of this patient's cutaneous and musculoskeletal symptoms is most similar to that of which of the following conditions?

A) Acute rheumatic fever
B) Drug-induced serum sickness
C) Graft-versus-host disease
D) Immune response to PPD skin testing
E) Peanut allergy

Correct Answer – B

The malar rash of systemic lupus erythematosus (SLE) is characterized by pink patches involving the malar cheeks and bridge of the nose that spare the nasolabial folds. SLE is an example of type III (immune complex–mediated) hypersensitivity reaction, which is defined by the presence of circulating antigen-antibody complexes that deposit in tissues. These complexes then bind and activate complement, which attracts neutrophils. The neutrophils set into motion an inflammatory cascade and release lysosomal enzymes, causing inflammation and degradation of the surrounding healthy tissue. Another example of type III hypersensitivity is serum sickness. Serum sickness occurs when a drug, such as anti-thymocyte globulin, acts as a hapten to the immune system, triggering antibody formation. The antibodies then bind the drug, deposit in tissue, and attract and activate complement. The result is fever, rash, and arthralgias. Serum sickness reaction usually occurs 1 to 2 weeks after the initial exposure to the drug, reflecting the time required to mount an immune response.

Incorrect Answers: A, C, D, and E.

Acute rheumatic fever (Choice A) is a late complication of untreated Group A *Streptococcus* infection characterized by carditis, subcutaneous nodules, erythema marginatum, Sydenham chorea, and migratory polyarthritis. The cause is related to immune cross-reactivity caused by molecular homology between streptococcal M protein and human cardiac myosin proteins. It is a type II (complement-mediated cytotoxic) hypersensitivity reaction.

Graft-versus-host disease (Choice C) and immune response to PPD skin testing (Choice D), or tuberculin reaction, are examples of type IV (delayed) hypersensitivity reactions. Type IV hypersensitivity is characterized by a cell-mediated response that involves the maturation of antigen-specific $CD4^+$ or $CD8^+$ T lymphocytes to a specific antigen. When the antigen is encountered, $CD4^+$ T lymphocytes release cytokines leading to inflammation and macrophage activation, while $CD8^+$ T lymphocytes directly kill cells expressing the antigen. This type of hypersensitivity takes several days to manifest. Allergic contact dermatitis is another example of a type IV hypersensitivity reaction.

Peanut allergy (Choice E) is an example of a type I (immediate) hypersensitivity reaction. Type I hypersensitivity occurs when preformed IgE on the surface of mast cells and basophils is crosslinked by an antigen, leading to immediate degranulation and release of histamine. This results in vasodilation, vascular pooling, and increased vascular permeability, which clinically manifests as urticaria, angioedema, or anaphylaxis.

Educational Objective:
Type III hypersensitivity is defined by the presence of circulating antigen-antibody-complement complexes that deposit in tissues and cause inflammation and destruction. SLE, serum sickness reaction, polyarteritis nodosa, and poststreptococcal glomerulonephritis are all examples of type III hypersensitivity reactions.

🧠 Key First Aid Summary Points

- SLE = Type III hypersensitivity (immune complex deposition)
- Low complement (↓C3, ↓C4) supports active immune complex disease
- Malar rash + arthritis = hallmark of SLE

🎯 NBME Question Strategy Tip

- Watch for malar rash, morning stiffness, and low complement → strongly suggests immune complex–mediated disease like serum sickness or SLE.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"Previously healthy 16-year-old girl… progressive rash over cheeks and bridge of nose"	Classic description of malar rash	+ Distribution (sparing nasolabial folds)	Lupus facial rash = sun-exposed areas
"1-week history of stiffness of her fingers in the mornings…"	Morning stiffness = inflammatory arthritis	+ Joint symptoms consistent with SLE	Nonerosive arthritis in lupus
"ANA titer of 1:1280"	ANA = highly sensitive test for lupus	+ Autoimmune marker	First-line lupus screening
"C3 concentration of 71 (N=100–200)"	Low complement → ongoing immune complex consumption	+ Classic SLE flare feature	Seen in active lupus nephritis, rash, or arthritis

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❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. Acute rheumatic fever	Type II hypersensitivity	Molecular mimicry, not immune complex deposition
✅ B. Drug-induced serum sickness	Type III hypersensitivity	Mechanism matches SLE: immune complex-mediated
C. Graft-versus-host disease	Type IV hypersensitivity	T-cell mediated; not relevant to ANA/rash/complement
D. Immune response to PPD	Type IV hypersensitivity	Delayed-type T-cell response; no immune complexes
E. Peanut allergy	Type I hypersensitivity	IgE-mediated and immediate—not immune complex based

📜 Illness Script: Pattern Recognition Aid

If you see malar rash + arthritis + ↓C3/C4 + ANA+ → then think SLE → immune complex deposition like serum sickness (Type III hypersensitivity)

NBME 23

A 70-year-old woman comes to the physician because of a 3-month history of increasingly severe pain of her joints. She says that her fingers have become so stiff that she can no longer play the piano. Physical examination shows rheumatoid nodules underneath the skin close to the joints of the elbows and hands. The immunologic mechanism of this patient's inflammation is most similar to which of the following?

A) Apoptosis of macrophages
B) Mast cell degranulation
C) Natural killer cell killing
D) Serum sickness
E) Wheal and flare reaction

Correct Answer – D

Serum Sickness. SS is a type 3 HS due to antibodies to foreign proteins, leading to antibody antigen complexes and complement activation causing inflammatory damage. You note fever, arthralgia, lymphadenopathym, and you run out of complement.
Rheumatoid Arthritis. RA is also a type 3 HS with IgM against IgG Fc region.

🧠 Key First Aid Summary Points

- Rheumatoid arthritis = Type III hypersensitivity
- Immune complexes activate complement → chronic synovial inflammation
- Associated with anti-CCP and rheumatoid factor (IgM vs IgG)

🎯 NBME Question Strategy Tip

- If you see joint pain + stiffness + rheumatoid nodules, don't just think of diagnosis—ask, *what immune process fits?* If it's chronic and systemic, immune complexes are likely involved.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"70-year-old woman… 3-month history of	Chronic polyarthritis	+ Duration >6 weeks	RA hallmark = symmetric polyarthritis

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
increasingly severe joint pain”			
“Fingers so stiff she can’t play piano”	Morning stiffness = inflammatory arthritis	+ Functional impact	>1 hour stiffness = autoimmune
“Rheumatoid nodules underneath skin near joints”	Classic extra-articular RA finding	+ Nodules = systemic immune activation	Indicates severe disease and immune complex involvement

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❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. Apoptosis of macrophages	Intracellular infection clearance	Not relevant to joint inflammation or nodules
B. Mast cell degranulation	Type I hypersensitivity	Immediate (e.g., allergies), not chronic joint disease
C. NK cell killing	Innate immunity (e.g., viral-infected cells)	No cytotoxicity or viral context
✅ D. Serum sickness	Type III hypersensitivity	Same immune complex/complement-mediated mechanism as RA
E. Wheal and flare	Type I hypersensitivity (histamine)	Immediate allergy, not chronic systemic disease

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🧻 Illness Script: Pattern Recognition Aid

If you see chronic symmetric joint pain + nodules + morning stiffness → then think rheumatoid arthritis → Type III hypersensitivity (immune complex–mediated)

NBME 18

A 39-year-old man comes to the physician because of a 1-week history of red spots on his shins, joint pain, and fatigue. His temperature is 37°C (98.6°F), and pulse is 74/min. Physical examination shows purpura over the lower extremities. The liver edge is palpated 4 cm below the right costal margin. Laboratory studies show:

- Leukocyte count: 10,000/mm³

- **Serum**
- AST: 142 U/L
- ALT: 154 U/L
- Hepatitis C virus RNA: positive
- Anti-hepatitis C virus antibody: positive
- Cryoglobulins: positive
- C4: 120 µg/mL (N = 350–600)

Urine

- Protein: 4+
- RBC: numerous

Which of the following types of hypersensitivity reactions is the primary cause of the renal damage in this patient?

○ A) Type I (Immediate)
○ B) Type II (complement-mediated cytotoxic)
✓ C) Type III (immune complex-mediated)
○ D) Type IV (delayed)

Why it's the right answer: There's a lot of information in this question and lot to learn. First, know that that skin reaction is called erythema nodosum and all the diseases that can present with it – i.e. IBD, sarcoid, TB, cat-scratch disease, etc. Basically, this is hepatitis C infection leading to liver abnormalities and cryoglobulinemia resulting in a nephrotic syndrome (the 4+ protein is grounds to push this from the category of nephritic syndrome into a nephrotic syndrome). The specific nephrotic syndrome is membranoproliferative glomerulonephritis, which is a nephritic syndrome but can copresent as a nephrotic syndrome. The cryoglobuminemia is the result of complement and immunoglobulins directing acting on an antigen (i.e. the kidney), and leading to a type III immune reaction. This question is great because it combines several organ systems and immunology, and the board examiners love getting more bang for their buck – or your buck rather!

Take home point: Cryoglobuminemia is a type III hypersensitivity reaction and causes membranoproliferative glomerulonephritis.

🧠 Key First Aid Summary Points

- HCV-associated cryoglobulinemia = Type III hypersensitivity
- Immune complexes deposit in small vessels → vasculitis, glomerulonephritis
- ↓Complement (esp. C4) is a diagnostic clue for immune complex disease

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🎯 NBME Question Strategy Tip

- Watch for purpura + renal damage + ↓C4 + cryoglobulins in an HCV+ patient → this is immune complex glomerulonephritis (Type III)

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"39-year-old man… red spots on shins, joint pain, fatigue"	Purpura + arthralgia + fatigue = vasculitis syndrome	+ Classic cryoglobulinemia triad	Cryoglobulins = small vessel vasculitis (Type III)
"Liver edge 4 cm below RCM"	Hepatomegaly = likely chronic hepatitis C	+ HCV risk	HCV commonly triggers cryoglobulinemia
"AST/ALT elevated; HCV RNA and antibodies positive"	Confirms active hepatitis C infection	+ Active HCV infection	Chronic antigenemia → immune complex formation
"Cryoglobulins: positive; C4: 120 (low)"	Cryoglobulins + ↓C4 = immune complex deposition	+ Type III hypersensitivity red flags	Key First Aid marker of cryo-associated vasculitis
"Urine: 4+ protein, numerous RBCs"	Nephritic + nephrotic features → GN	+ Immune-mediated glomerular damage	Immune complexes deposit in glomeruli (Type III)

❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect in This Vignette
A. Type I (Immediate)	IgE-mediated allergy (e.g., anaphylaxis)	No allergen exposure, no eosinophils, no urticaria
B. Type II (cytotoxic)	Antibody binding directly to cells (e.g., hemolysis)	No cell-surface antigen involved; this is circulating ICs
✅ C. Type III (immune complex-mediated)	Cryoglobulins deposit in glomeruli → vasculitis	HCV → immune complex disease → ↓C4, purpura, GN
D. Type IV (delayed)	T-cell mediated (e.g., contact dermatitis, TB)	No granulomas or delayed reaction signs; not cell-mediated

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📜 Illness Script: Pattern Recognition Aid

If you see HCV + purpura + low C4 + proteinuria/hematuria → then think cryoglobulinemic vasculitis → Type III hypersensitivity

Zaki

Type 4

NBME 30

A 55-year-old homeless man comes to the emergency department because of a 2-month history of intermittent fever, cough productive of blood-tinged sputum, night sweats, and fatigue; he has had a 3.2-kg (7-lb) weight loss due to decreased appetite during this period. On arrival, he is cachectic and has a chronic cough. His temperature is 38°C (100.4°F). Rhonchi are heard over the right upper lobe. A chest x-ray shows areas of cavitation in the right upper lobe. Which of the following is the most likely cause of tissue injury in this patient's condition?

A) Antigen-antibody complex deposition
B) Arthus reaction
C) Delayed-type hypersensitivity
D) Pseudomembrane formation
E) Wheal and flare reaction

Correct Answer: C.

Delayed-type hypersensitivity reaction, also known as a type IV hypersensitivity reaction, most likely accounts for this patient's lung injury in the setting of pulmonary tuberculosis. Type IV hypersensitivity is characterized by a cell-mediated response which involves maturation of antigen specific $CD4^+$ or $CD8^+$ T lymphocytes, which in this case, are antigens specific to *Mycobacterium tuberculosis* (MTB). When the antigen is encountered, $CD4^+$ T lymphocytes release cytokines leading to inflammation and macrophage activation, while $CD8^+$ T lymphocytes directly kill cells expressing the antigen. Activated macrophages become histiocytes and form granulomas, which in the case of MTB, may be caseating granulomas. Local inflammation at the site of MTB infection is an attempt to encapsulate and/or destroy MTB, but the local immune response results in substantial damage to the surrounding lung parenchyma.

Incorrect Answers: A, B, D, and E.

Antigen-antibody complex deposition (Choice A), also called a Type III hypersensitivity reaction, is a result of immune complex (antigen-antibody) deposition in tissues resulting in a local inflammatory response and complement fixation with subsequent damage to tissues. Common diseases in which this plays a role include polyarteritis nodosa, systemic lupus erythematosus, and serum sickness.

Arthus reaction (Choice B) is a localized type III (antigen-antibody complex) hypersensitivity reaction whereby complexes that fix complement deposit in blood vessels and cause local necrosis. It occasionally occurs with hepatitis B or tetanus vaccines, although this is uncommon.

Pseudomembrane formation (Choice D) occurs in infection with *Clostridium difficile*, a bacterium that causes colitis in patients with recent exposure to antibiotics. Colonoscopy classically shows pseudomembranes on the surface of colonic mucosa. Pseudomembrane formation is not a characteristic of MTB infection.

Wheal and flare reaction (Choice E) indicates the presence of mast cell degranulation and typically manifests as hives. The cause may be related to medication effects, heat or cold exposure, allergies, or may be idiopathic.

Educational Objective:
MTB infection induces a type IV (delayed-type) hypersensitivity reaction in which MTB antigens induce maturation of $CD4^+$ and $CD8^+$ T lymphocytes specific to that antigen. It results in a local inflammatory response, with direct cytotoxic killing of infected cells by $CD8^+$ T lymphocytes and stimulation of macrophage activation with subsequent granuloma formation.

🧠 Key First Aid Summary Points

- TB = Type IV hypersensitivity (cell-mediated)
- Granulomatous inflammation → tissue destruction
- $CD4^+$ T cells activate macrophages → caseating granulomas

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🎯 NBME Question Strategy Tip

- Cavitary lung lesion + weight loss + night sweats → *Think TB*
- Tissue damage in TB is not due to bacteria directly, but from immune-mediated granuloma formation

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🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"55-year-old homeless man…"	Risk factor: TB more common in homelessness	+ Vulnerable population	TB = reactivation in immunocompromised
"2-month history of fever, hemoptysis,	Systemic signs = chronic infection	+ Classic TB triad	Think reactivation TB

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
night sweats, fatigue”			
“Weight loss due to ↓ appetite”	Constitutional symptom of chronic infection	+ Cachexia = TB red flag	IL-1, TNF-α → appetite suppression
“Rhonchi in right upper lobe”	Pulmonary focus = cavitary TB likely	+ Apical disease	TB favors oxygen-rich upper lobes
“CXR: cavitation in RUL”	Cavitary lesion = TB hallmark	+ Granuloma breakdown	Caseating granuloma → cavitation = Type IV hypersensitivity damage

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❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It’s Incorrect Here
A. Antigen-antibody complex deposition	Type III hypersensitivity	Seen in lupus, serum sickness—not TB
B. Arthus reaction	Localized Type III hypersensitivity	Vaccine-related or localized—TB is systemic, not immune complex-based
✅ C. Delayed-type hypersensitivity	Type IV hypersensitivity	CD4+ T cell activation → granuloma → tissue destruction
D. Pseudomembrane formation	C. difficile infection	Colon pseudomembranes—not found in TB lungs
E. Wheal and flare reaction	Type I hypersensitivity	IgE-mediated; think allergies—not delayed granulomatous disease

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🧻 Illness Script: Pattern Recognition Aid

If you see chronic cough + night sweats + cavitation on CXR → then think TB → Type IV hypersensitivity with granulomatous inflammation

NBME 26

A 32-year-old woman comes to the physician because of a 3-month history of fevers, weakness, and night sweats. Physical examination shows enlarged axillary lymph nodes. A photomicrograph of tissue obtained on biopsy of an affected node is shown. A stain for acid-fast bacilli is negative. Which of the following is most likely involved in the pathogenesis of these findings?

A) Activation of alternate complement pathway
B) Streptococcal infection of the region drained by the lymph node
C) Type I (immediate) hypersensitivity reaction
D) Type III (immune complex-mediated) hypersensitivity reaction
E) Type IV (delayed) hypersensitivity reaction

Correct Answer – E

Type IV (delayed) hypersensitivity reaction is the correct answer. This patient with fevers, night sweats, and lymphadenopathy with a lymph node biopsy showing noncaseating granulomas likely has sarcoidosis, a disease with myriad manifestations that most commonly involves the lungs, eyes, skin, and central nervous system. It is characterized by granuloma formation in the absence of pathogenic microbes such as fungi or mycobacterium. The noncaseating epithelioid granulomas, which are the hallmark of sarcoidosis, are thought to contain an antigen at their core, with surrounding macrophages that form multinucleated giant cells. The dense lymphocytic inflammatory infiltrate that surrounds these granulomas contains many helper $CD4^+$ T lymphocytes, cytotoxic $CD8^+$ T lymphocytes, B lymphocytes, and fibroblasts. Granuloma formation is often a consequence of type IV hypersensitivity reactions, which involve the exposure of a sensitized individual to an antigen, followed 24 to 72 hours later by an immune reaction to the antigen. The response is primarily cellular rather than mediated by antibodies, and the cells involved are macrophages and Th_1 helper T cells. Thus, a type IV hypersensitivity reaction is consistent with granuloma formation in sarcoidosis.

Incorrect Answers: A, B, C, and D.

Activation of alternate complement pathway (Choice A) does not occur in sarcoidosis and has no role in the formation of granulomas. The alternate complement pathway has been implicated in the pathogenesis of atypical hemolytic uremic syndrome, among other diseases such as lupus nephritis.

Streptococcal infection of the region drained by the lymph node (Choice B) would not likely present with granulomas on lymph node biopsy. Bacterial infections commonly lead to a reactive lymph node profile with infiltration of the node by neutrophils.

Type I (immediate) hypersensitivity reaction (Choice C) is IgE-mediated and is the type of reaction that occurs in allergies and anaphylaxis. IgE antibodies are produced in response to an initial exposure to an antigen. With subsequent exposure, IgE antibodies cross-link on mast cells and basophils, resulting in immediate degranulation of these cells with the release of histamine, leukotriene, and prostaglandins.

Type III (immune complex-mediated) hypersensitivity reaction (Choice D) is a result of immune complex (antigen-antibody) deposition in tissues resulting in a local inflammatory response and complement fixation with subsequent damage to tissues. Common diseases in which this plays a role include polyarteritis nodosa, systemic lupus erythematosus, and serum sickness.

Educational Objective:
Sarcoidosis is characterized by the development of non-caseating granulomas, which is achieved via a type IV hypersensitivity reaction to an unknown antigen.

🧠 Key First Aid Summary Points

- Sarcoidosis = Type IV (delayed-type) hypersensitivity
- Noncaseating granulomas → $CD4^+$ T cell–mediated macrophage activation
- Negative AFB stain rules out TB or fungal causes

🎯 NBME Question Strategy Tip

- Granulomas = Think Type IV
- If biopsy shows noncaseating granulomas + systemic symptoms + AFB–, think sarcoidosis, not infection.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
“32-year-old woman… 3-month history of fevers, weakness, night sweats”	Constitutional symptoms → think chronic inflammatory/immune disease	+ Classic sarcoidosis prodrome	Sarcoid = systemic granulomatous inflammation

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"Enlarged axillary lymph nodes"	Lymphadenopathy → supports systemic process	+ Peripheral node involvement	Sarcoid often has intrathoracic + peripheral nodes
"Photomicrograph of biopsy…"	Biopsy = essential to identify granulomas	+ Diagnostic step	Histology distinguishes between TB vs sarcoidosis
"Stain for acid-fast bacilli is negative"	Excludes TB and mycobacteria	– TB or MAC	Noncaseating + AFB– = think sarcoidosis
"Which mechanism…"	Focus on pathogenesis, not just diagnosis	– Not antibody mediated	$CD4^+$ T cell → macrophage → granuloma = Type IV

❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect in This Vignette
A. Alternate complement pathway activation	Seen in aHUS, lupus nephritis	No complement-mediated injury here
B. Streptococcal infection	Reactive lymphadenitis	Doesn't form granulomas—neutrophilic not granulomatous
C. Type I hypersensitivity	IgE-mediated (e.g., anaphylaxis)	Not involved in granuloma or chronic T cell immunity
D. Type III hypersensitivity	Immune complex deposition	No circulating ICs; sarcoidosis is cell-mediated
✅ E. Type IV (delayed-type) hypersensitivity	$CD4^+$ T cells + macrophages = granulomas	Correct mechanism for sarcoidosis

📜 Illness Script: Pattern Recognition Aid

If you see constitutional symptoms + noncaseating granulomas + AFB negative → then think sarcoidosis → Type IV hypersensitivity

NBME 23

A 7-year-old boy is brought to the physician by his mother because of a 2-day history of an itchy red rash on his right arm and trunk after a hike in the woods. His mother says that the rash began on his arm 1 day after the trip, but it has now spread to his trunk. Physical examination shows 2-cm patches of raised, red, elongated blisters that ooze clear fluid on the upper extremities and trunk. The blisters are in a linear distribution with patches of erythema. Which of the following best describes the mechanism of this patient's reaction?

A) Activation of mast cells by IgE
B) Deposition of antigen-antibody complexes
C) Late phase reaction of a type I hypersensitivity
D) Release of interferon gamma by Th1 cells
E) Synthesis of high-affinity IgG by B lymphocytes

Correct Answer - D

Type 4 HS. The kid probably has a reaction to something like poison ivy or oaks from the woods. His symptoms are of contact dermatitis. Clearly the patient is responding to something with T cells not an antibody/antigen thing so it can't be types 1-3. Also, answer A is more related to asthma.

🧠 Key First Aid Summary Points

- **Contact dermatitis = Type IV hypersensitivity**
- **Mediated by Th1 cells → IFN-γ activates macrophages**
- **Linear vesicles = poison ivy/oak exposure pattern**

🎯 NBME Question Strategy Tip

- **Delayed-onset, pruritic, vesicular rash after environmental contact** → Think **Type IV**
- Watch for **linear lesions** → poison ivy/oak = classic boards buzzword

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🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"7-year-old boy… itchy red rash after a hike"	Environmental trigger = contact allergen	+ Outdoor exposure = poison ivy/oak	Allergens like urushiol (plant oil) trigger DTH

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"Rash began 1 day after the trip, now on trunk"	Delayed onset = excludes IgE/histamine	+ 24–48 hour delay	Type IV takes 1–3 days to develop
"2-cm raised, red, elongated blisters… linear distribution"	**Classic poison ivy/oak description**	+ Vesicles + linear streaks	Allergen spreads on skin via scratching/contact

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❌ **Distractor Analysis Table**

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. Activation of mast cells by IgE	Type I hypersensitivity (allergies)	Onset is immediate, not delayed by 1–2 days
B. Deposition of antigen-antibody complexes	Type III hypersensitivity	Seen in SLE, serum sickness—not contact dermatitis
C. Late phase of Type I hypersensitivity	Still IgE-driven → hours later	Wrong mechanism—this is T-cell mediated
☑ **D. Release of IFN-γ by Th1 cells**	**Type IV hypersensitivity** → activates macrophages	Correct mechanism in poison ivy/oak reactions
E. Synthesis of high-affinity IgG by B cells	Humoral/antibody production	IgG plays no role in contact dermatitis

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📋 **Illness Script: Pattern Recognition Aid**

If you see linear vesicular rash after plant contact with 24–48 hour delay → **then think** contact dermatitis → **Th1 cell activation → IFN-γ → Type IV hypersensitivity**

NBME 22

A 23-year-old woman develops multiple red, papulovesicular lesions following exposure to poison ivy. Which of the following is the most likely mechanism underlying the development of these lesions?

A) Allergen-mediated vasoconstriction, leading to ischemic tissue injury
B) Binding of antigen to IgE on the surface of mast cells, leading to mast cell degranulation
C) Deposition of antigen-antibody complexes within postcapillary venules, leading to activation of complement
D) Phagocytosis of antigen by neutrophils, leading to oxidant-mediated tissue damage
E) Processing of antigen by Langerhans cells, leading to activation of $CD4^+$ T cells

Correct Answer – E

Poison ivy triggers a type IV hypersensitivity (mediated by T cells); only one of the answer choices mentions T cells. Poison ivy, nickel, and some other similar things cause contact dermatitis. Graft vs Host is also a type 4 response.

🧠 Key First Aid Summary Points

- **Poison ivy = Type IV hypersensitivity**
- **Antigen processed by Langerhans cells (skin dendritic cells)**
- **$CD4^+$ Th1 cells → IFN-γ → macrophage recruitment and tissue injury**

🎯 NBME Question Strategy Tip

- **Papulovesicular rash + delayed onset + plant exposure** → this is **cell-mediated**, not antibody-mediated.
- Know that **Langerhans cells** = skin APCs = activate **$CD4^+$ T cells** in Type IV reactions.

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"23-year-old woman develops red, papulovesicular lesions…"	Vesicular rash = inflammation of dermis/epidermis	+ Classic contact dermatitis morphology	Poison ivy = urushiol oil triggers Type IV DTH

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"Following exposure to poison ivy"	Allergen contact = delayed response	+ Strong environmental trigger	Contact dermatitis from plant oils is hallmark Type IV
"Most likely mechanism?"	Focus on immune activation cascade	– Not IgE or antibody	T-cell mediated → no role for antibodies here

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❌ **Distractor Analysis Table**

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. Vasoconstriction–mediated ischemia	Vascular ischemia (e.g., Raynaud's)	Not part of hypersensitivity; no ischemic injury in contact dermatitis
B. IgE + mast cell degranulation	Type I hypersensitivity	Immediate allergy (e.g., urticaria, anaphylaxis) – wrong timing & mechanism
C. Immune complex deposition	Type III hypersensitivity	Seen in lupus, serum sickness – not contact dermatitis
D. Neutrophil phagocytosis + oxidant damage	Acute bacterial infection	Not the mechanism of delayed T-cell-mediated hypersensitivity
☑ **E. Langerhans cell activation → $CD4^+$ T cells**	**Type IV hypersensitivity**	Correct: APC presents antigen → activates Th1 cells → cytokines → rash

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📝 **Illness Script: Pattern Recognition Aid**

If you see vesicular rash after poison ivy contact → **then think** contact dermatitis → **Langerhans cell → $CD4^+$ T cell activation → Type IV**

NBME 17

A 24-year-old man comes to the physician because of a 2-day history of an itchy rash on his arms and legs. He returned from a camping trip in the woods 5 days ago. Examination of the upper and lower extremities shows a widespread edematous, erythematous rash with linear vesicles. The most likely cause of these findings is activation of which of the following cell types?

A) B lymphocytes
B) Mast cells
C) Natural killer cells
D) Neutrophils
E) T lymphocytes

Correct Answer - E

Why it's right: The diagnosis is contact dermatitis from contact with poison ivy. Even if you thought this was possibly sporothrix schenckii ("rose handler's disease") since it can also cause a rash that is linear and vesicular, this is a question about hypersensitivity reactions, and it's hinting at poison ivy and a type IV hypersensitivity reaction. The rash is also on his arms and legs, which is less likely due to rose handler's disease that would be confined to the hands and arms. The key cell mediator of type IV hypersensitivity reactions is the T lymphocyte. T lymphocytes activate macrophages and there is no antibody involvement. Other type IV hypersensitivity examples include contact dermatitis due to nickel, PPDtest, graft-versus-host disease, multiple sclerosis, and Guillain-Barre syndrome.

Take home point: Poison ivy causes contact dermatitis, a type IV hypersensitivity reaction.

🧠 **Key First Aid Summary Points**

- **Type IV hypersensitivity = T cell–mediated (delayed)**
- **Linear vesicles + erythema = poison ivy/oak (urushiol exposure)**
- **No antibodies involved (not B cells or IgE)**

🎯 **NBME Question Strategy Tip**

- A **delayed itchy vesicular rash after camping** = *not immediate allergy*
- Always think **T cells (especially $CD4^+$ Th1) → IFN-γ → macrophages → inflammation**

🔍 Vignette Breakdown Table

Vignette Sentence	What to Think Clinically	Pertinent Positive/Negative	First Aid Integration
"24-year-old man… itchy rash on arms and legs"	Pruritic dermatitis = inflammatory skin reaction	+ Common distribution for contact allergen	Delayed-type hypersensitivity trigger
"Returned from a camping trip 5 days ago"	Environmental exposure to plants	+ Strongly suggests poison ivy/oak	Urushiol → skin allergen
"Widespread edematous, erythematous rash with linear vesicles"	**Classic poison ivy rash** → contact dermatitis	+ Linear vesicles	Type IV → T-cell mediated skin inflammation

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❌ Distractor Analysis Table

Answer Choice	Alluded Mechanism	Why It's Incorrect Here
A. B lymphocytes	Antibody production	No antibody involvement in delayed hypersensitivity
B. Mast cells	Type I hypersensitivity	Immediate reactions (hives, anaphylaxis) → not this
C. NK cells	Viral defense, tumor surveillance	No role in poison ivy/contact dermatitis
D. Neutrophils	Acute inflammation, bacterial infections	Not the driver of T cell–mediated hypersensitivity
✅ **E. T lymphocytes**	**Type IV hypersensitivity** → $CD4^+$ Th1 cells	Correct: contact allergens processed by APCs → activate T cells

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🧻 Illness Script: Pattern Recognition Aid

If you see vesicular, linear rash days after plant exposure → **then think** poison ivy → **T-cell mediated Type IV hypersensitivity**